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Isolated Lymph Node T Lymphoblastic Transformation of Chronic Myeloid Leukemia During Interferon Treatment

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Isolated nodal T lymphoblastic transformation of chronic myeloid leukemia (CML) with the marrow still in chronic phase is rare. A case of CML treated by α-interferon developed this unusual complication. However, after successful treatment of the blastic transformation, the patient remained responsive to interferon and maintained a major cytogenetic response for over 2 years. This case illustrated a rare clinical progression of CML on interferon treatment to isolated nodal T lymphoblastic transformation. This unusual form of blastic transformation may have a better prognosis than other forms of blastic crisis. Am. J. Hematol. 62:256–258, 1999. © 1999 Wiley-Liss, Inc.

Key words: T lymphoblastic lymphoma; chronic myeloid leukemia

INTRODUCTION

Chronic myeloid leukemia (CML) evolves ultimately from a chronic phase into blastic crisis. Allogeneic bone marrow transplantation is a curative treatment for suitable patients. In patients who are not candidates for transplantation, the use of α-interferon (IFN-α) results in improvement in survival, particularly in patients in whom the Philadelphia chromosome (Ph) positive clone is suppressed [1].

However, when CML enters blastic transformation (BT), the prognosis is extremely poor, with an overall survival of less than 5 months [2]. About 30% of CML-BTs are lymphoid, of which most are of B lineage [2,3], so that T lineage blastic crisis is very uncommon. The median survival of patients with lymphoid BT was poor at 10 months [3]. Interestingly, lymphoid BT appeared to occur more frequently in patients responding to IFN treatment [4].

CML-BT occurs predominantly in the marrow, but a small number of cases undergo extramedullary BT [5]. We describe a patient with CML undergoing IFN-α treatment, who developed the rare complication of an isolated extramedullary T lymphoblastic transformation. This patient was further intriguing in showing a prolonged survival after effective treatment of the lymphoblastic transformation.

METHODS AND RESULTS

Case Report

A 50-year-old Chinese man presented 54 months ago with chronic myeloid leukemia in chronic phase. IFN-α was administered (3–6 megaunits/day), resulting in a good control of his white cell count. Twenty-nine months after presentation the patient developed an isolated right supraclavicular nodal T lymphoblastic BT. A bone marrow biopsy showed CML still in chronic phase. He was treated with combination chemotherapy consisting of cyclophosphamide (600 mg/m^2), adriamycin (50 mg/m^2/day × 3), vincristine (2 mg/week × 4), and prednisolone (60 mg/day × 28), which resulted in a complete remission. With the nodal transformation in complete remission, IFN-α treatment was recommenced. The patient achieved a complete hematologic remission and a major cytogenetic response and has remained in chronic phase for 25 months since BT. He is currently evaluated for autologous bone marrow transplantation.

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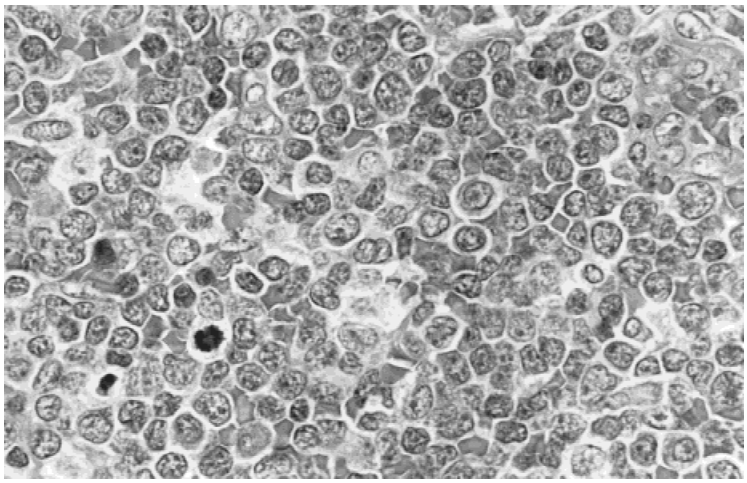

Fig. 1. Microscopic examination of the lymph node showed diffuse infiltration by small- to medium-sized blasts with round nuclear outline, fine chromatin, and scanty cytoplasm (original magnification 500×).

TABLE I. Results of Cytogenetic and Fluorescence In Situ Hybridization Studies

Time (months)	Event	Karyotype: No. of cells	Karyotype: % of cells normal	Karyotype: % of cells t(9;22)	FISH for M*BCR/ABL*: No. of cells scored	FISH for M*BCR/ABL*: % of cells Indeterminate[a]	FISH for M*BCR/ABL*: % of cells Negative[b]	FISH for M*BCR/ABL*: % of cells Positive[c]
1	IFN 3 MU	ND	–	–	ND[d]	–	–	–
3	IFN 6 MU	25	60	40	ND	–	–	–
5	–	25	64.0	36.0	200	9.5	26	64.5
8	–	34	44.2	55.8	200	7.5	8.5	84
12	–	4	0	100	200	5.5	7.0	87.5
14	IFN 9 MU	–						
23		51	23.5	76.5	200	10.5	14.5	75.0
29	T-LB[e]	–						
30	Chemo[f]	–						
31	–	25	96.0	4.0	200	8.0	87.0	5
34	CR	28	100	0	ND	–	–	–
43	IFN 6 MU	ND	–	–	100	10.0	64.0	26.0
52	IFN 6 MU	25	88	12	200	8.0	62.0	30.0
54	IFN 9 MU	4	100	0	50[g]	4.0	78.0	18.0

[a]Indeterminate: cells with less or more than 2 red (BCR) and 2 green (ABL) fluorescence signals.
[b]Negative: cells with two red and two green signals.
[c]Positive: cells with an unequivocal red and green fusion signal, and one of each of green and red signal.
[d]ND: not done.
[e]T-LB: T lymphoblastic nodal transformation.
[f]Chemotherapy: combination chemotherapy.
[g]Only 50 cells were scored, because marrow aspiration was difficult and only very few cells could be obtained.

Histologic and Immunophenotypic Studies

The lymph node was diffusely infiltrated by blasts with round to ovoid nuclei of fine chromatin and scanty cytoplasm (Fig. 1). Immunophenotyping showed an immature T-cell phenotype: terminal deoxynucleotidyl transferase +, CD1−, CD2+, CD3+, CD4−, CD5+, CD7+, CD8−. The blasts were negative for myeloperoxidase and CD10, CD19, and CD22.

Cytogenetic, Fluorescence In Situ Hybridization (FISH) and Molecular Studies

The initial diagnostic marrow showed t(9;22)(q34;q11) without additional karyotypic abnormalities. Reverse transcription polymerase chain reaction for *BCR/ABL* was performed as previously reported [6] and confirmed a b3a2 fusion (data not shown). FISH for BCR/ABL was performed with a M*BCR/ABL* probe mix (Oncor, Gaithersburg, MD) as described [7]. The serial results are shown in Table I. There was an initial cytogenetic response, but a gradual expansion of the Ph positive clone heralded T lymphoblastic transformation. Interestingly, a suppression of the Ph positive clone occurred after induction chemotherapy of the T lymphoblastic transformation. The subsequent IFN-α treatment resulted again in a major cytogenetic response (Table I), up to the latest assessment 25 months after BT.

DISCUSSION

During the blastic phase of CML, lymphoid BT appeared to be more frequent than myeloid BT in interferon responders [4]. Lymphoid BT were predominantly of B lineage, with less than twenty cases involving the T cell lineage ever been reported [3,8]. Most of these cases presented as marrow blastic transformation with variable involvement of lymph nodes. To our knowledge, only one case presented as isolated nodal T lymphoblastic transformation, with the marrow still in chronic phase [9], which was similar to our patient. Interestingly, in both cases IFN treatment was given. The emergence of this rare complication of extramedullary BT in CML after IFN treatment had been partly attributed to an alteration in the course of the medullary disease in CML which, because of the prolongation of the chronic phase as a result of IFN therapy, allowed the development of the unusual extramedullary course [10].

Furthermore, this patient illustrated other interesting features. Firstly, the T lymphoblastic BT showed an unusually long remission of more than 25 months, which was in sharp contrast to the reported median survival of 10 months in medullary lymphoid BT [4]. This suggests that isolated extramedullary BT may have a better prognosis. Secondly, the marrow had apparently still retained IFN responsiveness despite BT. The maintenance of a chronic phase in the marrow also affirmed the absence of marrow involvement during the BT.

In summary, this case reiterated the more frequent occurrence of lymphoid BT in CML patients responding to IFN, with our patient being unusual in showing a T lymphoid BT in an extramedullary site. The prolonged survival and favorable response to IFN treatment suggest that isolated extramedullary BT may have a better prognosis than medullary BT. Further studies in this rare group of patients, including the use of high-dose chemotherapy and allogeneic or autologous stem cell rescue, are warranted.

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